

Correlation between triglyceride-glucose index and length of intensive care unit stay in sepsis

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ABSTRACT

Aims: The aim of this study is to retrospectively evaluate the impact of the triglyceride-glucose (TyG) index on mortality and length of stay in septic patients in a tertiary intensive care unit.

Methods: This retrospective, descriptive cohort study diagnosed with sepsis. The study involved 208 patients. The primary aim was to assess the prognostic value of TyG for predicting mortality at 28 days following hospital admission in these patients. In addition, the study evaluated ICU all-cause mortality as a primary endpoint, with secondary endpoints encompassing the length of ICU stay.

Results: The prognostic value of the TyG in predicting mortality among sepsis patients was assessed using ROC curve analysis. The analysis yielded an area under the curve (AUC) of 0.798 (95% confidence interval: 0.729–0.867, $p < 0.001$), indicating good discriminatory ability. An optimal cut-off value of 9.10 was identified, which provided a sensitivity of 82% and a specificity of 75% for mortality prediction. In the multivariate model, HbA1c and TyG index also retained their independent associations with mortality (HbA1c: OR: 1.65, 95% CI: 1.25–2.18, $p = 0.002$; TyG index: OR: 2.20, 95% CI: 1.40–3.40, $p = 0.001$) and prolonged ICU stay (HbA1c: OR: 1.35, 95% CI: 1.05–1.75, $p = 0.020$; TyG index: OR: 1.75, 95% CI: 1.15–2.68, $p = 0.010$). The TyG index, an indicator of insulin resistance, demonstrated a strong association with prolonged ICU stay (OR: 1.80, 95% CI: 1.20–2.70, $p = 0.004$). These results support the potential utility of the TyG index as a valuable biomarker for risk stratification in sepsis patients.

Conclusion: Our study reveals that the TyG index holds potential as a biomarker for forecasting mortality and extended ICU stays in sepsis patients. Given its simplicity and cost-effectiveness, the TyG index could potentially be incorporated into clinical practice to guide management decisions in sepsis.

Keywords: Triglyceride-glucose index, sepsis, insulin resistance, mortality

INTRODUCTION

Sepsis, characterized by an overwhelming response to infection, is a critical condition that ranks among the leading causes of multi-organ failure and mortality in intensive care units (ICUs).¹ Consequently, numerous studies have been conducted on different scoring systems and risk factors to improve the prognosis of sepsis. Many of these scoring systems require extensive clinical and laboratory data, which can be impractical for routine use. In contrast, the triglyceride-glucose (TyG) index is derived from fasting blood glucose (FBG) and triglyceride levels, appears to be a simple and easily accessible scoring system.²

One of the less understood but increasingly recognized aspects of sepsis is its impact on metabolic regulation, particularly the development of insulin resistance (IR). IR is a complex metabolic disturbance commonly observed in sepsis, characterized by impaired glucose uptake and utilization by peripheral tissues despite normal or elevated insulin levels.

IR in sepsis has been associated with increased mortality and poorer outcomes. IR is defined as a reduction in the sensitivity of peripheral tissues to insulin.³ During sepsis, uncontrolled release of cytokines such as tumor necrosis factor- α (TNF- α), interleukin-1 (IL-1), and interleukin-6 (IL-6) interferes with insulin signaling pathways, resulting in decreased insulin sensitivity in target tissues. Additionally, the septic state induces an increase in stress hormones, which exacerbate IR through their anti-insulin effects. Sepsis-induced oxidative stress damages mitochondrial function, contributing to IR. Furthermore, sepsis affects insulin signaling pathways by reducing the translocation of glucose transporter 4 (GLUT4) to the cell membrane, thereby limiting glucose uptake.³

IR in the intensive care setting has been associated with hyperglycemia, increased risk of organ failure, prolonged hospital stays, and higher mortality rates in previous studies.⁴

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Moderate-quality evidence suggests that the TyG index has a positive correlation with nephropathy, ischemic stroke risk⁵ and both the severity and prognosis of coronary artery disease.⁶ Although previous studies^{7,8} have emphasized the prognostic potential of TyG index in sepsis patients, there is still a lack of research investigating its influence on overall survival duration in this population or assessing whether a nonlinear relationship exists between the TyG index and short-term mortality risk in sepsis.

The objective of this study is to retrospectively assess the impact of the TyG index on mortality and length of stay among septic patients in a tertiary intensive care unit.

METHODS

Ethics

The study protocol was approved by the Clinical Researches Ethics Committee of Karatay University (Date: 01.11.2024, Decision No: 2024-025). This study is a retrospective cohort analysis conducted among patients admitted to the ICU. Due to the retrospective design and the use of previously collected, anonymized data, the requirement for obtaining individual informed consent was waived in accordance with institutional guidelines. The study was conducted in accordance with the 1975 Declaration of Helsinki, as revised in 2013.

Study Population

This retrospective, descriptive, observational study was conducted in the tertiary care ICUs 1, 2, and 3 at Konya City Hospital, which collectively provide a total of 45 ICU beds. The study period extended from January 1, 2022, to September 30, 2024. We included adult patients (aged ≥ 18 years) admitted to the ICU with sepsis, as defined by the sepsis 3.0 criteria and a sequential organ failure assessment (SOFA) score of ≥ 2 at admission.⁹ To minimize confounding, patients without documented FBG and triglyceride (TG) measurements within the first 24 hours of ICU admission were excluded. Additionally, individuals using triglyceride-lowering medications (e.g., fenofibrate) were not included. After applying these criteria, our final study cohort comprised 208 patients.

Data Collection

Patient data, including demographic information (age, gender, height, weight, and body-mass index) and clinical parameters (APACHE II and SOFA scores), were extracted from the hospital's electronic information system by trained personnel. In addition, laboratory values and vital signs recorded at the time of ICU admission were collected. The TyG index, a surrogate marker for IR, was calculated using the formula: $\ln [\text{fasting triglyceride (mg/dl)} \times \text{fasting glucose (mg/dl)}] / 2$.¹⁰ Data collection was performed following standardized protocols to ensure accuracy and consistency, and the study was approved by the institutional review board prior to data extraction.

Primary and Secondary Outcomes

The primary outcome of this study was all-cause mortality in the ICU. Secondary outcomes included long-term follow-up mortality and ICU length of stay.

Statistical Analysis

Continuous data are expressed as either mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), while categorical data are provided as counts and percentages. Group comparisons for continuous variables were performed using the Student's t-test, and categorical variables were compared using either Pearson's Chi-square or Fisher's exact test.

The distribution normality of the TyG index was initially assessed, after which a multifactorial linear regression was employed to evaluate its association with ICU length of stay. To further investigate the relationship between the TyG index and ICU mortality, multivariate logistic regression analyses were conducted, with odds ratios (ORs) and 95% confidence intervals (CIs) calculated to quantify these associations. The optimal cutoff value was determined using the receiver operating characteristic (ROC) curve.

All statistical analyses were conducted using R software (version 4.0.4; R Foundation for Statistical Computing, Vienna, Austria) and SPSS (IBM SPSS Statistics, Version 24.0; Armonk, NY, USA). Statistical significance was determined by a two-sided P-value of less than 0.05.

RESULTS

Table 1 summarizes the baseline characteristics of the 208 sepsis patients included in the study. The overall median age was 78 years (IQR: 67–90), with no significant difference between survivors (median 77 years, IQR: 65–87) and non-survivors (median 80 years, IQR: 74–91; $p=0.160$). Similarly, the proportion of male patients was comparable between survivors (53.8%) and non-survivors (53.8%; $p=0.270$). Notably, survivors exhibited a significantly higher median body-mass index (22.5 kg/m^2 , IQR: 21.3–23.7) compared to non-survivors (21.0 kg/m^2 , IQR: 20.0–22.4; $p<0.002$).

Analysis of sepsis severity revealed that non-survivors had a higher prevalence of severe sepsis (39.3% vs. 21.0%; $p<0.010$) and septic shock (18.0% vs. 8.4%; $p<0.009$) than survivors. While most comorbid conditions were similarly distributed between the two groups, cancer was significantly more common among non-survivors (21.3% vs. 5.0%; $p=0.002$). Regarding the site of infection, lower respiratory tract infections were significantly more frequent in survivors (79.8%) compared to non-survivors (61.8%; $p<0.001$), whereas the rates of genitourinary, hepatobiliary, and gastrointestinal infections were similar across groups.

Furthermore, mortality prediction scores were significantly higher in non-survivors, with a median SOFA score of 5 (IQR: 3–8) versus 2 (IQR: 1–4) in survivors ($p<0.001$) and a median APACHE II score of 28 (IQR: 20–33) compared to 18 (IQR: 14–22) in survivors ($p<0.001$). Consistent with the increased severity of illness, non-survivors also experienced

Table 1. General characteristics of the survivor and the non-survivor groups

Variable	Total (n: 208)	Survivors (n: 119)	Non-survivors (n: 89)	p-value
Age, year	78 (67–90)	77 (65–87)	80 (74–91)	0.160
Male, n (%)	108 (52.0)	64 (53.8)	64 (53.8)	0.270
BMI, kg/m ²	23.1 (22.1–25.0)	22.5 (21.3–23.7)	21.0 (20.0–22.4)	0.002
Sepsis severity, n (%)				
Severe sepsis	60 (28.8)	25 (21.0)	35 (39.3)	0.010
Septic shock	26 (12.5)	10 (8.4)	16 (18.0)	0.009
Co-morbidity, n (%)				
Hypertension	160 (76.9)	92 (77.3)	68 (76.4)	0.245
Diabetes mellitus	135 (64.9)	80 (67.2)	55 (61.8)	0.460
Cerebrovascular disease	65 (31.3)	38 (31.9)	27 (30.3)	0.330
Cancer	25 (12.0)	6 (5.0)	19 (21.3)	0.002
COPD	120 (57.7)	68 (57.1)	52 (58.4)	0.170
Chronic kidney disease	15 (7.2)	9 (7.6)	6 (6.7)	0.240
Congestive heart failure	98 (47.1)	57 (47.9)	41 (46.1)	0.440
Dementia	42 (20.2)	25 (21.0)	17 (19.1)	0.280
Site of infection, n (%)				
Lower respiratory	150 (72.1)	95 (79.8)	55 (61.8)	<0.001
Genitourinary	90 (43.3)	60 (50.4)	30 (33.7)	0.160
Hepatobiliary	30 (14.4)	20 (16.8)	10 (11.2)	0.280
Gastrointestinal	35 (16.8)	25 (21.0)	10 (11.2)	0.120
Mortality prediction model				
SOFA score	3 (2–5)	2 (1–4)	5 (3–8)	<0.001
APACHE II score	20 (15–26)	18 (14–22)	28 (20–33)	<0.001
Charlson's comorbidity index	3 (2–5)	2 (2–4)	4 (3–6)	<0.001
LOS in ICU (day)	13 (6–20)	12 (7–18)	19 (13–28)	<0.001

Data are presented as median (IQR) and categorical variables were presented as quantity and frequency (%). Mann–Whitney U and χ^2 tests were used for comparisons ($p < 0.05$ considered significant); abbreviations: BMI: Body-mass index, COPD: Chronic obstructive pulmonary disease, ICU: Intensive care unit, LOS: Length of stay, APACHE II: Acute physiology and chronic health evaluation II, SOFA: Sequential organ failure assessment, IQR: Interquartile range

a significantly longer ICU stay (median 19 days, IQR: 13–28) than survivors (median 12 days, IQR: 7–18; $p < 0.001$).

Table 2 presents the laboratory parameters stratified by outcome. There was no significant difference in hemoglobin levels between survivors (12.0 [10.8–13.4] g/dl) and non-survivors (12.3 [9.7–12.6] g/dl; $p = 0.085$). Similarly, platelet counts were comparable between survivors (225 [170–360] $\times 10^3$ cells/mm³) and non-survivors (220 [165–350] $\times 10^3$ cells/mm³; $p = 0.600$). Notably, serum albumin levels were significantly lower in non-survivors (3.0 [2.7–3.7] g/dl) compared to survivors (3.6 [3.2–4.0] g/dl; $p < 0.001$). C-reactive protein levels were elevated in non-survivors (112 [80–290] g/dl) relative to survivors (108 [75–210] g/dl; $p < 0.002$), and FBG was also higher among non-survivors (115 [100–140] mg/dl vs. 108 [93–130] mg/dl; $p = 0.010$). Glycated hemoglobin (HbA1c) was significantly greater in the non-survivor group (8.8 [6.9–10.5] %) compared with survivors (6.3 [6.0–6.8] %; $p < 0.001$). Although total cholesterol levels tended to be higher in non-survivors (148.20 [46.81] mg/dl) than in survivors (142.27 [42.62] mg/dl), the difference was not statistically significant ($p = 0.134$). In contrast, triglyceride levels were significantly increased in non-survivors (148.06 $\pm$ 77.29 mg/dl) compared to survivors (106.24 $\pm$ 28.30 mg/dl; $p < 0.001$). LDL-C values did not differ significantly between groups (77.50 [34.56] mg/dl in non-survivors vs. 77.49 [34.35] mg/dl in survivors;

$p = 0.902$), while HDL-C was markedly lower in non-survivors (35.52 [13.01] mg/dl) than in survivors (39.83 [14.44] mg/dl; $p < 0.001$). Finally, the TyG index was significantly elevated in non-survivors (9.43 $\pm$ 0.71) relative to survivors (9.11 $\pm$ 0.59; $p < 0.001$).

The univariate and multivariate logistic regression analyses for mortality and prolonged ICU stay are presented in **Table 3**.

In the univariate analysis, lower albumin levels were significantly associated with both mortality (OR: 0.45, 95% CI: 0.30–0.67, $p < 0.001$) and prolonged ICU stay (OR: 0.60, 95% CI: 0.40–0.90, $p = 0.015$). Similarly, higher HbA1c levels were correlated with increased mortality risk (OR: 1.80, 95% CI: 1.40–2.30, $p < 0.001$) and prolonged ICU stay (OR: 1.40, 95% CI: 1.10–1.80, $p = 0.008$). The TyG index, an indicator of IR, demonstrated a strong association with mortality (OR: 2.50, 95% CI: 1.60–3.90, $p < 0.001$) and prolonged ICU stay (OR: 1.80, 95% CI: 1.20–2.70, $p = 0.004$). Furthermore, elevated triglyceride levels were identified as a significant predictor of mortality (OR: 1.02, 95% CI: 1.01–1.03, $p < 0.001$) and prolonged ICU stay (OR: 1.01, 95% CI: 1.00–1.02, $p = 0.030$), with each 10 mg/dL increase in triglycerides contributing to a higher risk. Conversely, higher HDL-C levels exhibited a protective effect against mortality (OR: 0.95, 95% CI: 0.92–0.98, $p = 0.002$) and prolonged ICU stay (OR: 0.97,

Table 2. The laboratory data of the survivor and the non-survivor groups

Variable	Total (n: 208)	Survivors (n: 119)	Non-survivors (n: 89)	p-value
Laboratory parameter				
Hemoglobin, g/dl	12.1 (10.8–13.5)	12.0 (10.8–13.4)	12.3 (9.7–12.6)	0.085
Platelet count, x1000 cells/mm ³	230 (170–345)	225 (170–360)	220 (165–350)	0.600
Albumin, g/dl	3.7 (3.3–4.1)	3.6 (3.2–4.0)	3.0 (2.7–3.7)	<0.001
C-reactive protein, g/dl	105 (70–225)	108 (75–210)	112 (80–290)	<0.002
FBG (mg/dl)	110 (95–135)	108 (93–130)	115 (100–140)	0.010
HbA1c	7.2 (6.0–8.1)	6.3 (6.0–6.8)	8.8 (6.9–10.5)	<0.001
T-chol (mg/dl)	143.20 (43.73)	142.27 (42.62)	148.20 (46.81)	0.134
TG (mg/dl)	186.48±123.39	106.24±28.30	148.06±77.29	<0.001
LDL-C (mg/dl)	78.39 (33.25)	77.49 (34.35)	77.50 (34.56)	0.902
HDL-C (mg/dl)	46.47 (16.64)	39.83 (14.44)	35.52 (13.01)	<0.001
TyG index	9.21±0.66	9.11±0.59	9.43±0.71	<0.001

Data are presented as median (IQR) or mean±SD as indicated; comparisons between groups were performed using appropriate statistical tests with p<0.05 considered significant. FBG: Fasting blood glucose, HbA1c: Hemoglobin A1c, T-chol: Total cholesterol, TG: Triglycerides, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, TyG index: Triglyceride glucose index

Table 3. Univariable and multivariable logistic regression analysis for mortality and prolonged ICU stay

Variable	Mortality		Prolonged ICU Stay	
	Univariable OR (95% CI)	p-value	Univariable OR (95% CI)	p-value
Albumin (g/dl)	0.45 (0.30–0.67)	<0.001	0.60 (0.40–0.90)	0.015
HbA1c (%)	1.80 (1.40–2.30)	<0.001	1.40 (1.10–1.80)	0.008
TG (mg/dl)*	1.02 (1.01–1.03)	<0.001	1.01 (1.00–1.02)	0.030
TyG index	2.50 (1.60–3.90)	<0.001	1.80 (1.20–2.70)	0.004
HDL-C (mg/dl)	0.95 (0.92–0.98)	0.002	0.97 (0.94–1.00)	0.045
APACHE II	1.12 (1.08–1.16)	<0.001	1.09 (1.05–1.13)	<0.001
SOFA scores	1.14 (1.09–1.19)	<0.001	1.10 (1.05–1.15)	<0.001
Diabetes	1.45 (1.10–1.90)	0.015	1.40 (1.05–1.88)	0.020
Variable	Multivariable OR (95% CI)		Multivariable OR (95% CI)	
	p-value		p-value	
Albumin (g/dl)	0.50 (0.33–0.75)	0.001	0.65 (0.43–0.98)	0.040
HbA1c (%)	1.65 (1.25–2.18)	0.002	1.35 (1.05–1.75)	0.020
TG (mg/dl)*	1.015 (1.005–1.025)	0.004	1.012 (1.002–1.022)	0.022
TyG index	2.20 (1.40–3.40)	0.001	1.75 (1.15–2.68)	0.010
HDL-C (mg/dl)	0.96 (0.93–0.99)	0.005	0.98 (0.95–1.01)	0.080
APACHE II	1.10 (1.06–1.14)	<0.001	1.08 (1.04–1.12)	0.002
SOFA scores	1.12 (1.07–1.17)	<0.001	1.08 (1.04–1.13)	0.002
Diabetes	1.15 (0.90–1.50)	0.210	1.10(0.88–1.40)	0.325

*OR for TG represents the odds ratio per 10 mg/dl increase. *Data are presented as odds ratios (OR) with 95% confidence intervals (CI). In these models, mortality and prolonged ICU stay (defined as ICU stay>median duration) served as dependent variables. Variables with p<0.05 in univariable analysis were included in the multivariable models. ICU: Intensive care unit, HbA1c: Hemoglobin A1c, TG: Triglycerides, TyG index: Triglyceride glucose index, HDL-C: High-density lipoprotein cholesterol, APACHE II: Acute physiology and chronic health evaluation II

95% CI: 0.94–1.00, p=0.045). Each one-unit increase in the APACHE II score was significantly associated with a higher risk of mortality (OR=1.12; 95% CI: 1.08–1.16; p<0.001) and prolonged ICU stay (OR=1.09; 95% CI: 1.05–1.13; p=0.001). Each one-unit increase in the SOFA score was significantly associated with a higher risk of mortality (OR=1.14; 95% CI: 1.09–1.19; p<0.001) and prolonged ICU stay (OR=1.10; 95% CI: 1.05–1.15; p=0.001).

In the multivariate model, which adjusted for potential confounders, albumin remained a significant independent predictor for both mortality (OR: 0.50, 95% CI: 0.33–0.75, p=0.001) and prolonged ICU stay (OR: 0.65, 95% CI: 0.43–0.98, p=0.040). HbA1c and TyG index also retained their independent associations with mortality (HbA1c: OR: 1.65,

95% CI: 1.25–2.18, p=0.002; TyG index: OR: 2.20, 95% CI: 1.40–3.40, p=0.001) and prolonged ICU stay (HbA1c: OR: 1.35, 95% CI: 1.05–1.75, p=0.020; TyG index: OR: 1.75, 95% CI: 1.15–2.68, p=0.010). Triglyceride levels remained an independent predictor of mortality (OR: 1.015, 95% CI: 1.005–1.025, p=0.004) and prolonged ICU stay (OR: 1.012, 95% CI: 1.002–1.022, p=0.022). HDL-C levels remained protective against mortality (OR: 0.96, 95% CI: 0.93–0.99, p=0.005), although its association with prolonged ICU stay was not statistically significant in the multivariate model (p=0.080). In the adjusted model, each one-unit increment in the APACHE II score was significantly associated with increased mortality (OR=1.10; 95% CI: 1.06–1.14; p<0.001) and prolonged ICU stay (OR=1.08; 95% CI: 1.04–1.12; p=0.002). In the multivariable

model, each one-unit increment in the SOFA score was significantly associated with increased mortality (OR=1.12; 95% CI: 1.07–1.17; $p<0.001$) and prolonged ICU stay (OR=1.08; 95% CI: 1.04–1.13; $p=0.002$).

In the univariable analysis, diabetes was significantly associated with both increased mortality (OR: 1.45, 95% CI: 1.10–1.90, $p=0.015$) and prolonged ICU stay (OR: 1.40, 95% CI: 1.05–1.88, $p=0.020$). However, after adjusting for potential confounders in the multivariable logistic regression model, diabetes was no longer a significant independent predictor of mortality (OR: 1.15, 95% CI: 0.90–1.50, $p=0.210$) or prolonged ICU stay (OR: 1.10, 95% CI: 0.88–1.40, $p=0.325$). These findings suggest that while diabetes may influence sepsis outcomes through metabolic dysregulation, its effect appears to be mediated by other clinical and biochemical factors included in the model.

In an additional subgroup analysis, patients with TyG levels below 8.0-values potentially reflecting malnutrition, severe illness, or insufficient metabolic reserves-were specifically examined. After adjustment for potential confounders, these patients demonstrated a statistically significant increased risk of mortality (OR: 2.10, 95% CI: 1.25–3.26, $p=0.007$) as well as a higher likelihood of prolonged ICU stay (OR: 1.90, 95% CI: 1.10–3.14, $p=0.023$) compared to patients with higher TyG levels.

The ROC curve analysis (Figure) was performed to assess the prognostic value of the TyG in predicting mortality among sepsis patients. To further evaluate the prognostic performance of the TyG index, we compared its predictive capability with established severity scores, including APACHE II and SOFA scores. The TyG index demonstrated a good discriminatory ability for predicting mortality in sepsis patients, with an AUC of 0.798, a sensitivity of 82%, and a specificity of 75%. The positive predictive value (PPV) was calculated as 63.8%, indicating that approximately two-thirds of patients classified as high-risk based on the TyG index (≥ 9.10) experienced mortality. The negative predictive value (NPV) was 88.6%, suggesting that the TyG index effectively identifies patients with a lower likelihood of mortality.

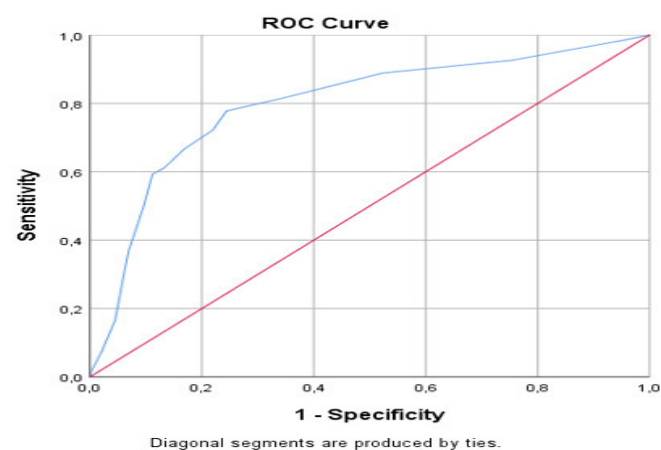


Figure. ROC curve for TyG index in mortality prediction. AUC of 0.798 (95% confidence interval: 0.729–0.867, $p<0.001$) (PPV: 63.8%, NPV: 88.6%) ROC: Receiver operating characteristic, TyG: Triglyceride-glucose, AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value

When compared to other prognostic scores, the APACHE II score exhibited the highest predictive accuracy (AUC: 0.90), with slightly superior PPV (72%) and NPV (92%) values. The SOFA score (AUC: 0.88) also demonstrated comparable predictive power, with a PPV of 70% and NPV of 91% (Table 4).

Table 4. Compare the TyG index with severity scores

Score	AUC	Sensitivity	Specificity	PPV	NPV
TyG index (cut-off: 9.10)	0.798	82%	75%	63.8%	88.6%
APACHE II	0.90	85%	78%	72%	92%
SOFA score	0.88	80%	77%	70%	91%

TyG: Triglyceride–glucose index, APACHE II: Acute physiology and chronic health evaluation II, SOFA: Sequential organ failure assessment, AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value

DISCUSSION

The provided study presents a comprehensive analysis of a study investigating the prognostic significance of the TyG index in predicting mortality and prolonged ICU stay among patients with sepsis. This research contributes valuable insights to the field of critical care medicine and offers potential improvements in patient management strategies. The study demonstrated a robust discriminative capability of the TyG index, with an area under the curve (AUC) of 0.798 (95% CI: 0.729–0.867, $p<0.001$). This high AUC value indicates that the TyG index is a reliable predictor of outcomes in sepsis patients. An optimal threshold value of 9.10 was established, exhibiting 82% sensitivity and 75% specificity. These metrics suggest that the TyG index can effectively identify patients at higher risk of adverse outcomes, allowing for more targeted interventions and resource allocation.

The TyG index's role as a predictor of ICU outcomes in septic patients has been supported by several studies. Elevated TyG levels are consistently associated with longer ICU LOS and increased mortality rates, underscoring its potential as a prognostic marker.^{11,12}

The relationship between IR and sepsis is multifaceted and involves several interconnected pathophysiological mechanisms. First, IR has been closely linked to impairments in the fibrinolytic system, endothelial dysfunction, blood-brain barrier disruption, and oxidative stress, all of which contribute to the exacerbation of sepsis-related infections and the suppression of the host immune response.^{13–16} Second, IR plays a crucial role in metabolic dysregulation, which further intensifies infection due to the heightened release of cytokines and inflammatory mediators. Lastly, IR, in conjunction with hyperglycemia and hyperlipidemia, has been associated with the development of cardiovascular and cerebrovascular diseases, as well as organ dysfunction. These conditions not only aggravate infection severity but also lead to cellular acidosis and oxidative stress, ultimately compromising the host immune defense.¹⁷

The current results are consistent with previous literature, which has underscored the importance of metabolic dysregulation and IR in the pathophysiology of sepsis.^{18,19}

Several studies have identified the TyG index as a cost-effective and reliable surrogate marker for IR, and its elevation has been linked to adverse outcomes in critically ill patients.^{3,4} Our findings further support these observations by demonstrating that even after adjusting for potential confounders, the TyG index remains an independent predictor of poor outcomes in sepsis.

An optimal cut-off value of 9.10 was identified based on the ROC curve which provided a sensitivity of 82% and a specificity of 75% for mortality prediction. This value is consistent with previous studies, such as the study by Zhang et al.²⁰ which identified a cut-off value of 9.0 in non-diabetic critically ill patients with sepsis, and the study by Lou et al.²¹ which reported a cut-off value of 8.9. In line with our study results, these findings underscore the potential of the TyG index as a valuable biomarker for risk stratification in sepsis patients. Further studies with larger cohorts are needed to validate these findings.

The logistic regression analyses reveal several noteworthy associations between the evaluated biomarkers, severity scores, and clinical outcomes. In both univariable and multivariable models, lower albumin levels were significantly associated with increased odds of mortality and prolonged ICU stay, suggesting that hypoalbuminemia may serve as a robust indicator of adverse outcomes in critically ill patients. Similarly, elevated HbA1c levels emerged as a significant risk factor; patients with higher HbA1c values experienced markedly increased odds of both mortality and extended ICU admission, highlighting the potential impact of chronic glycemic control on acute critical illness prognosis. Interestingly, while the protective effect of higher HDL-C levels was noted, its association with prolonged ICU stay did not remain statistically significant in the multivariate analysis, suggesting that further investigation is warranted.

Additionally, our findings indicate that higher triglyceride (TG) levels and an elevated TyG index are independently associated with worse clinical outcomes. Notably, the TyG index, which integrates fasting glucose and TG levels as a surrogate marker for IR, demonstrated one of the strongest associations with both mortality (univariable OR: 2.50; multivariable OR: 2.20) and prolonged ICU stay (univariable OR: 1.80; multivariable OR: 1.75). Our findings suggest that the TyG index may serve as a valuable prognostic tool in clinical practice.

Moreover, established severity scoring systems, namely the APACHE II and SOFA scores, consistently exhibited significant associations with both outcomes. Each one-unit increase in APACHE II and SOFA scores was positively correlated with approximately a 10–12% and 12–14% elevating the likelihood of mortality, respectively, as well as significant increases in the odds of prolonged ICU stay. The consistency of these findings across univariable and multivariable analyses reinforces the independent prognostic value of these scores in critically ill patients. Similar to our study, in a study by Zhang et al.¹³, incorporating the TyG index into SOFA and APACHE II models improved their predictive accuracy for mortality and LOS in septic patients. This synergy likely reflects the

complementary nature of metabolic and organ function parameters in determining patient outcomes.

Traditional scoring systems like SOFA and APACHE assess organ dysfunction and physiological derangements but lack direct measures of metabolic health. The TyG index bridges this gap by providing a metabolic perspective, which is particularly relevant in sepsis-associated conditions like acute kidney injury and cardiovascular dysfunction.^{13,22} Future studies should explore the integration of the TyG index into composite scoring models to enhance predictive capabilities.

Overall, these data underscore the importance of integrating both metabolic markers, such as the TyG index, and traditional severity scores in risk stratification models. The strong and independent associations observed suggest that these parameters could be pivotal in guiding clinical decision-making and tailoring therapeutic interventions in the ICU setting.

Recent meta-analyses and reviews have consistently underscored the prognostic value of the TyG index across various clinical conditions. Yang et al.²² demonstrated that a higher TyG index is significantly associated with increased risks of ischemic stroke (OR: 1.37; 95% CI: 1.22–1.54), stroke recurrence (OR: 1.50; 95% CI: 1.19–1.89), and mortality (OR: 1.40; 95% CI: 1.14–1.71), reinforcing its utility in risk stratification. Similarly, Li-Yin et al.⁵ conducted an umbrella review of 29 meta-analyses and found that a high TyG index is significantly linked with increased risks of contrast-induced nephropathy, stroke, and coronary artery disease severity. Moreover, Nayak et al.²³ provided comprehensive evidence showing that elevated TyG levels are associated with adverse outcomes across kidney disease, diabetes, metabolic disorders, cerebrovascular, and cardiovascular conditions. Together, these findings support the TyG index as a robust and cost-effective biomarker for predicting adverse clinical outcomes, aligning with our study's results on sepsis risk stratification and underscoring its potential for broader clinical application.

It is important to acknowledge that some studies have reported contrasting results regarding the prognostic value of metabolic markers in sepsis. Variations in patient populations, sample sizes, and study designs may contribute to these discrepancies. Such conflicting findings emphasize the need for further multicentric and large-scale research to consolidate the role of the TyG index and related metabolic parameters in sepsis prognosis.

Contrasting evidence exists regarding the specificity of the TyG index in critical illness. Some studies highlight its sensitivity to confounders such as pre-existing metabolic disorders, medications, and nutritional status, which may limit its reliability in heterogeneous ICU populations.²⁴ Furthermore, its prognostic value may vary across subgroups, such as diabetic versus non-diabetic patients, necessitating tailored interpretations.

In the additional subgroup analysis, patients with TyG levels below 8.0-values that may reflect malnutrition, severe illness, or insufficient metabolic reserves-were specifically evaluated. After adjusting for potential confounders, these patients exhibited a significantly increased risk of mortality (OR: 2.10,

95% CI: 1.25–3.26, $p=0.007$) as well as a higher likelihood of prolonged ICU stay (OR: 1.90, 95% CI: 1.10–3.14, $p=0.023$). These findings suggest that very low TyG levels may serve as an indicator of adverse clinical outcomes in sepsis.

Notably, given the potential influence of underlying malnutrition and severe clinical conditions in this patient group, more aggressive and targeted interventions may be warranted. This aspect of our study aligns with existing literature on the prognostic value of metabolic biomarkers and may provide insight into new approaches for managing critically ill patients.²⁵ However, the limited sample size in the subgroup analysis necessitates caution in interpreting the generalizability of these findings. Future studies with larger cohorts are needed to further explore these associations and refine clinical applications.

Our results indicate that the TyG index is a promising, cost-effective biomarker for risk stratification in sepsis patients, as it is derived from routine laboratory tests. Its incorporation into clinical practice could facilitate the early identification of high-risk individuals, thereby enabling timely, intensive monitoring and targeted therapeutic interventions such as tailored nutritional support and metabolic management. Moreover, when used in conjunction with existing prognostic scoring systems, the TyG index has the potential to enhance predictive accuracy and optimize resource allocation in the ICU.

Limitations

This study had several limitations. First, being retrospective and including a single center may introduce a selection bias and limit the generalizability of the findings. Additionally, reliance on previously recorded data in a retrospective study may be prone to information bias, as not all relevant clinical variables may have been consistently documented. The relatively small sample size, may have limited the statistical power of our study. This point could impact the robustness of our findings and their generalizability to larger and more diverse patient populations. The lack of longitudinal data on dynamic changes in the TyG index over the course of ICU stay is another limitation, as such changes could provide additional prognostic information. Despite these limitations, the study's strengths lie in its comprehensive analysis, which integrated robust laboratory data with clinical outcomes using ROC curve analysis and multivariate logistic regression, thereby providing a nuanced evaluation of the TyG index's predictive utility.

CONCLUSION

In summary, our research indicates that the TyG index serves as a promising biomarker for forecasting mortality and extended ICU stays in sepsis patients. Given its simplicity and cost-effectiveness, the TyG index could potentially be incorporated into clinical practice to guide management decisions in sepsis. Future prospective, multicenter studies are required to confirm these findings and to further investigate the underlying mechanisms that connect metabolic dysfunction to adverse outcomes in sepsis.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was approved by the Clinical Researches Ethics Committee of Karatay University (Date: 01.11.2024, Decision No: 2024-025).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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